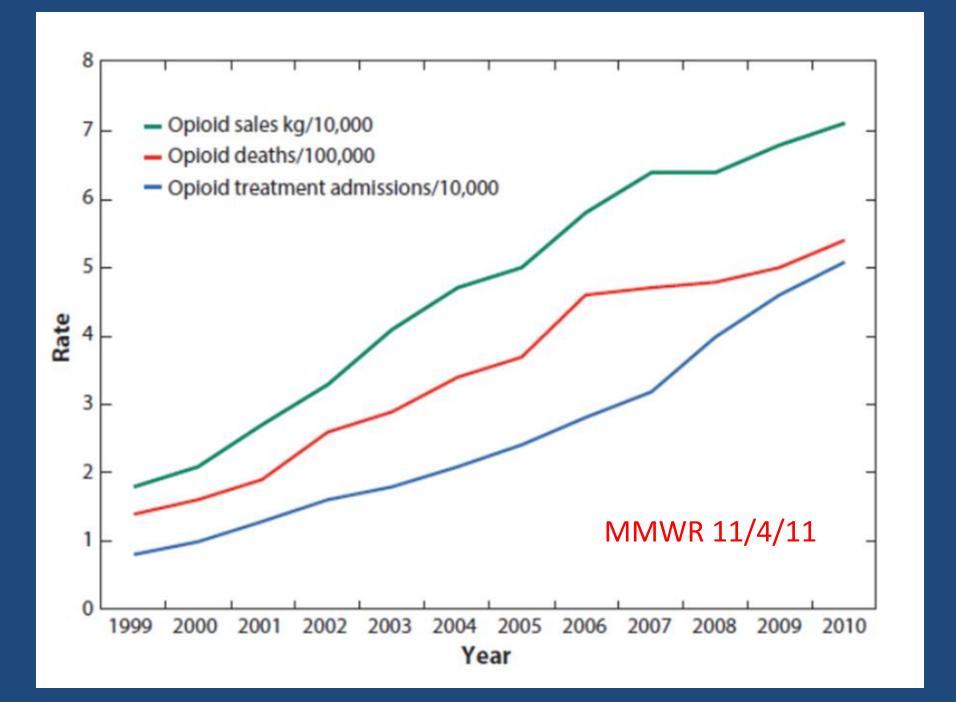
Caring for Chronic Pain within Addiction Treatment

Mishka Terplan MD MPH FACOG DFASAM
Addiction Medicine Specialist
DMAS

The Current Opioid Crisis:

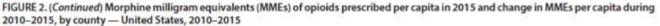
latrogenic

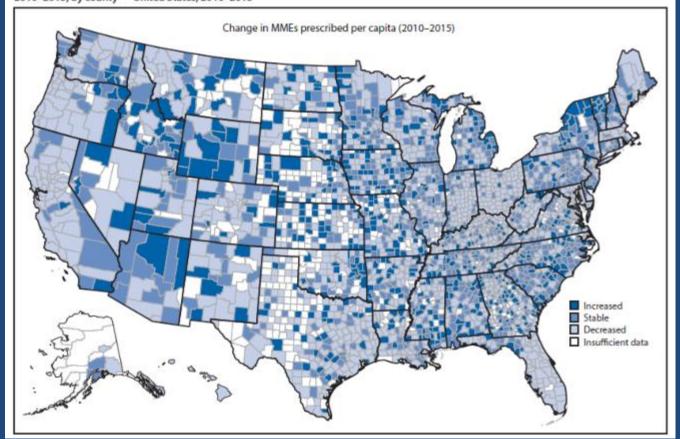


MMWR / July 7, 2017 / Vol. 66 / No. 26

Gery P. Guy Jr., PhD¹; Kun Zhang, PhD¹; Michele K. Bohm, MPH¹; Jan Losby, PhD¹; Brian Lewis²; Randall Young, MA²; Louise B. Murphy, PhD³; Deborah Dowell, MD¹

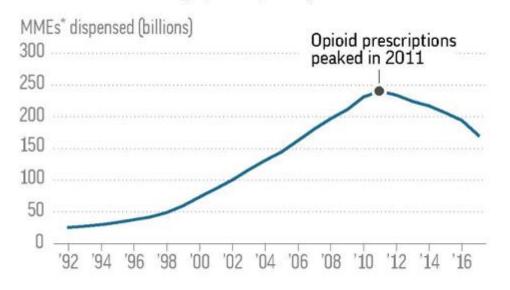
Prescription Opioid Epidemic Has Peaked Peak Opioid MME in US 782 (2010); 2015 = 640





Opioid prescriptions drop

Opioid prescriptions declined 12 percent from 2016 to 2017, the biggest single-year drop in 25 years.



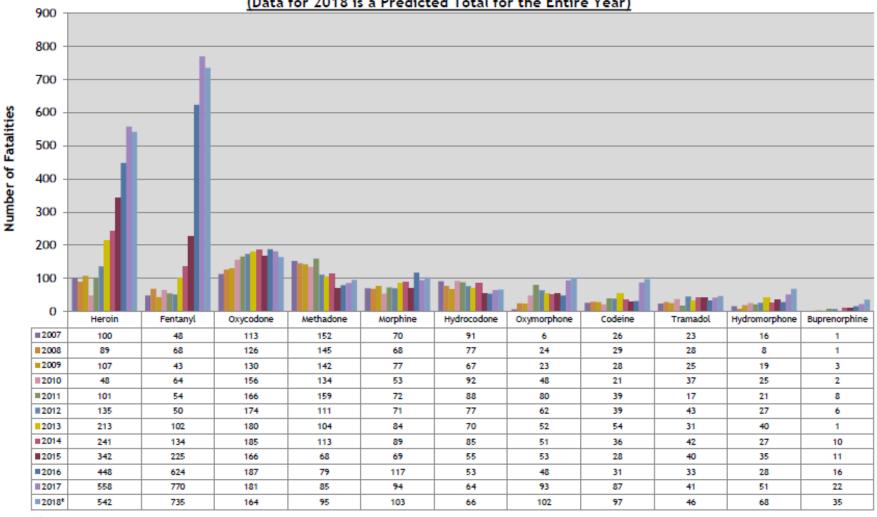
*Opioid doses are measured in morphine milligram equivalents. A standard Vicodin pill has the equivalent of 5 milligrams of morphine.

SOURCE: IQVIA's Institute for Human Data Science



ALL OPIOIDS

Total Number of Fatal Opioid Overdoses by Drug Name and Year of Death, 2007-2018 (Data for 2018 is a Predicted Total for the Entire Year)



¹ Illicit and pharmaceutically produced fatal fentanyl overdoses are represented in this analysis. This includes all different types of fentanyl analogs (acetyl fentanyl, furanyl fentanyl, etc.)



² Levorphanol, meperidine, pentazocine, propoxyphene, and tapentadol were excluded from this analysis due low annual case counts (<20 deaths)</p>

What is the risk of opioid addiction among individuals prescribed opioids for pain?

Rates of misuse 12-29% (95%CI:13-38%)

Rates of addiction 8-12% (95% CI: 3-17%)



Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis

Kevin E. Vowles^{a,*}, Mindy L. McEntee^a, Peter Siyahhan Julnes^a, Tessa Frohe^a, John P. Ney^b, David N. van der Goes^c

April 2015 • Volume 156 • Number 4

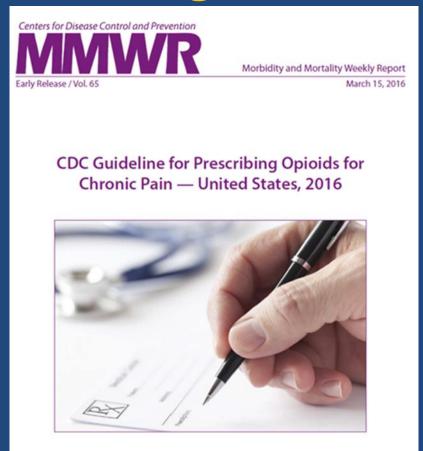
Table 4

Opioid addiction—unweighted and weighted means, SD, and 95% confidence interval (CI).

	Minimum, %		Maximum, %			
	Mean (SD)	95% CI	Mean (SD)	95% CI		
Unweighted	10.9 (9.8)	5.3-16.5	11.7 (9.9)	6.1-17.3		
Weighted means						
Sample size	4.3 (6.2)	0.8-7.8	4.7 (6.5)	1.0-8.4		
Log sample size	10.1 (9.5)	4.7-15.5	10.8 (9.6)	5.4-16.2		
Winsorized	7.8 (8.2)	3.2-12.4	8.6 (8.3)	3.9-13.3		
Quality rating	10.5 (8.8)	5.5-15.5	10.4 (8.9)	5.4-15.4		
Sample size × quality*	9.9 (8.7)	5.0-14.8	10.7 (8.9)	5.7-15.7		
Quality						
High-quality studies	8.8 (7.3)	4.3-13.3	9.8 (7.8)	5.0-14.6		
Low-quality studies	23.1 (12.9)	3.4-39.2	23.1 (12.9)	3.4-39.2		

^{&#}x27;Interaction term the product of standardized scores for the log transformed sample size and quality rating

The Opioid Crisis: Public Health Response Reduce Opioid Exposure through Opioid Prescribing Guidelines



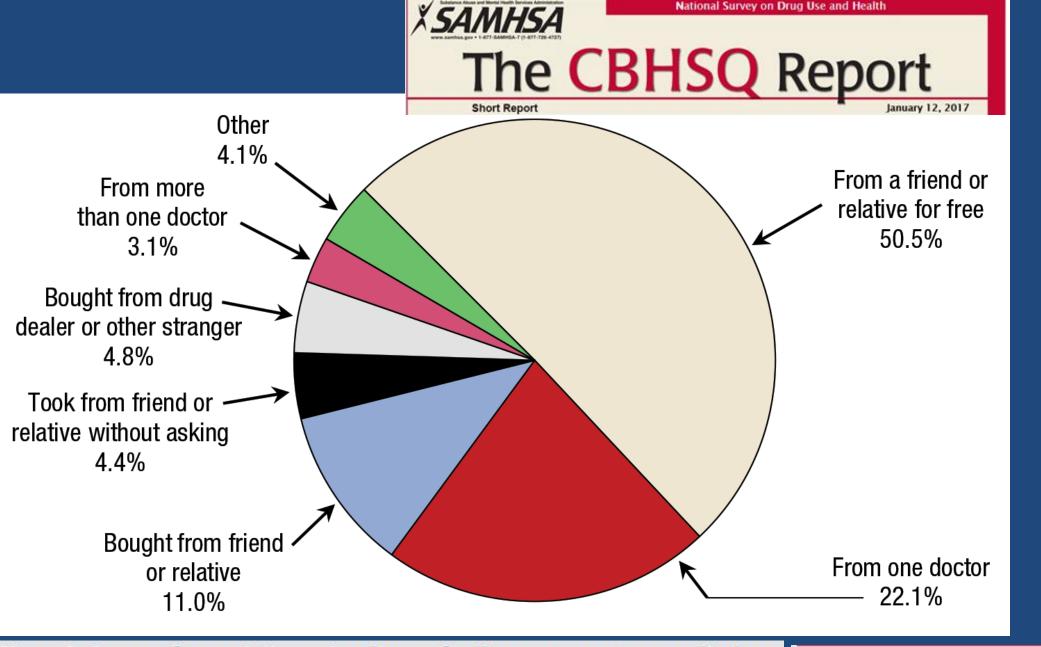


Figure 1. Source of prescription pain relievers for the most recent nonmedical use among past year users aged 12 or older: annual averages, 2013 and 2014

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Surveys on Drug Use and Health (NSDUHs), 2013 and 2014.

ORIGINAL ARTICLE

Safer and more appropriate opioid prescribing: a large healthcare system's comprehensive approach

Jan L. Losby PhD, MSW¹ | Joel D. Hyatt MD³ | Michael H. Kanter MD, CPPS⁴ | Grant Baldwin PhD, MPH² | Denis Matsuoka PharmD⁵

Guidelines Decrease Prescribing

Focusing on MME (or dose) reduction mirrors early epidemic focus on achieving lower pain score

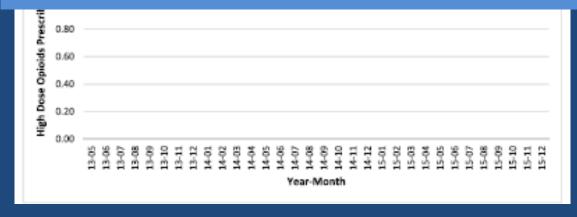


FIGURE 2 Opioid prescribing greater than or equal to 120 morphine milligram equivalent per day, per 1000 members per month

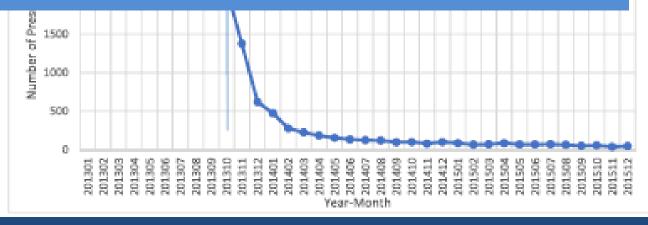
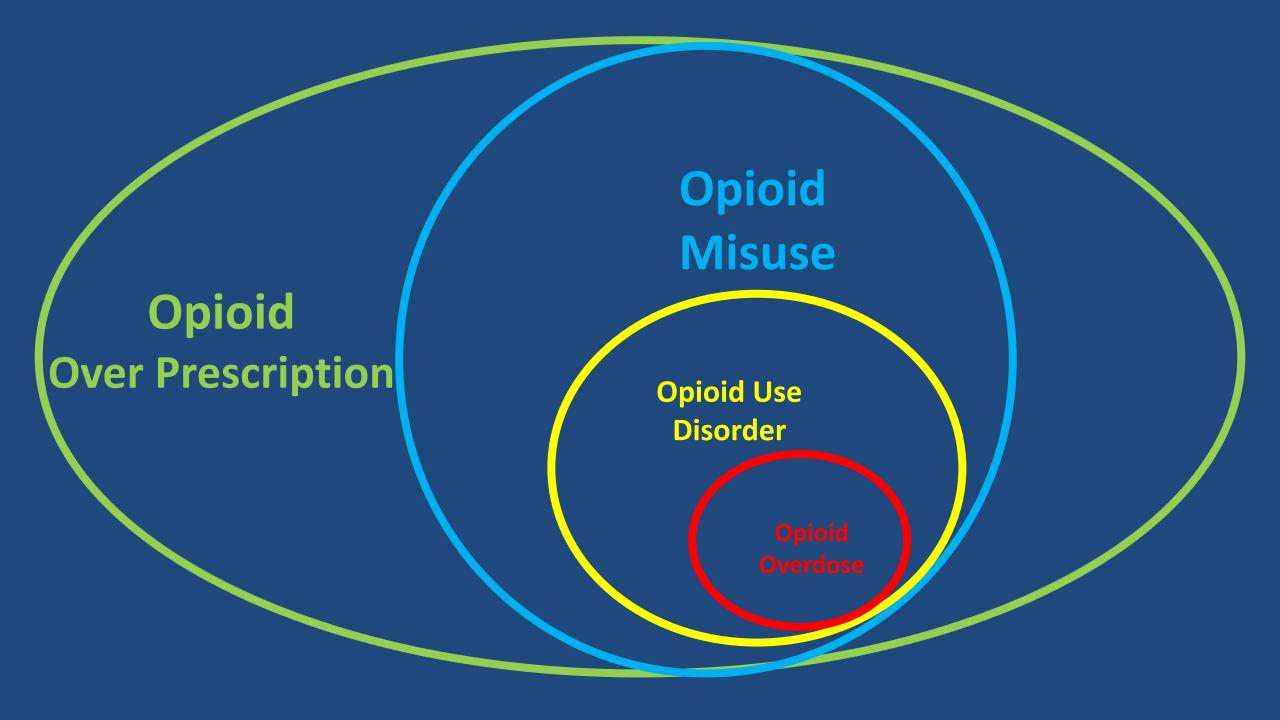
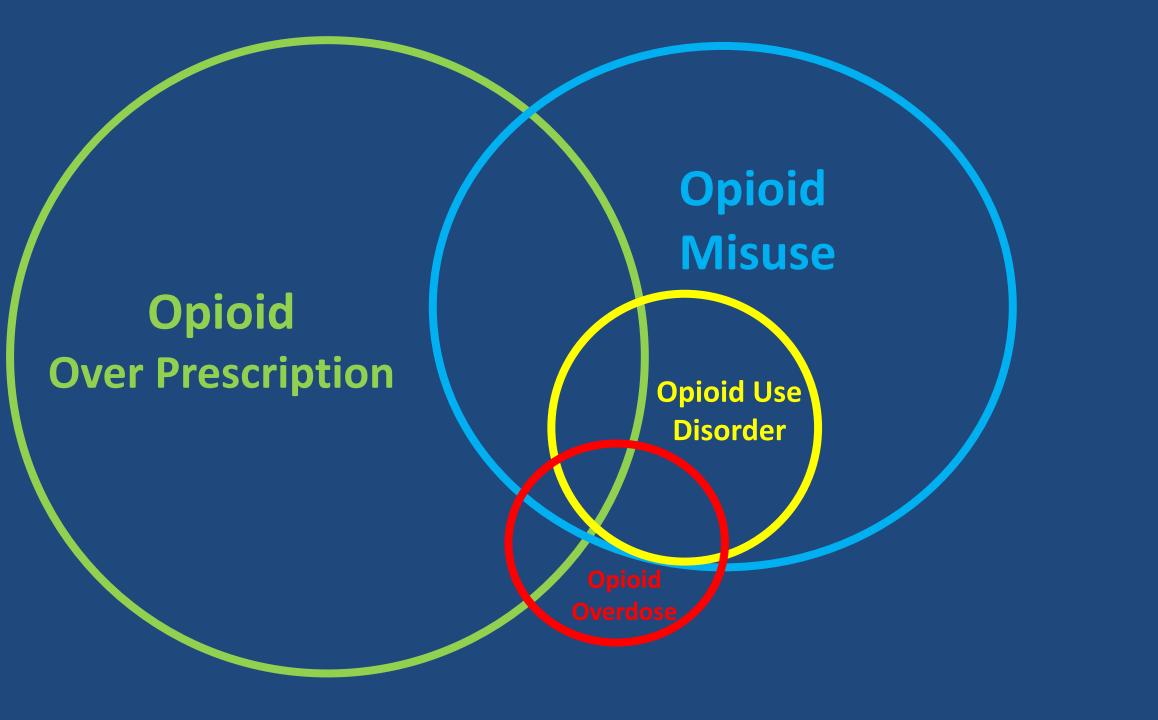


FIGURE 1 Number of opioid-acetaminophen prescriptions greater than 200 pills per prescription by month

Opioid Prescribing Guidelines







Addiction (?) in individuals with chronic pain

Opioid Taper

Non-Adherent With Taper

Refer to Addiction Provider

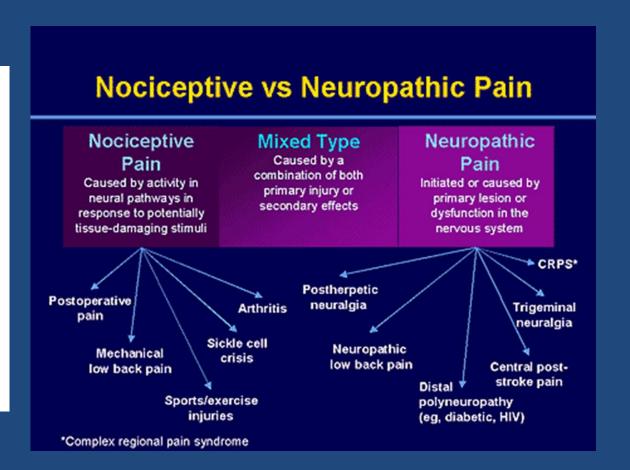
Addiction (?) in individuals with chronic pain

Screen for Addiction Refer for Treatment

Opioid Taper

Brief Intro to Pain Physiology

Туре	Description				
Nociceptive Pain	Pain that results from suprathreshold stimulation of nociceptors, which are neural receptors specialized for the detection of potentially harmful situations. This is an adaptive function of the nervous system. Nociceptors can be excited by mechanical, thermal, or chemical stimulation. The immediate physical response is reflexive and protective, causing a person to pull a hand away from a hot surface, for example. Nociceptive pain persists while the injurious agent remains or until healing occurs. Prolonged nociceptive input can cause central hypersensitization and the experience of spontaneous or amplified pain.				
Neuropathic Pain	Pain that results from lesion or dysfunction of the sensory nervous system. A compressed, injured, or severed nerve can trigger neuropathic pain, as can disorders that affect the neural axis (e.g., metabolic diseases, infections, autoimmune disorders, vascular diseases, neoplasia [Campbell & Meyer, 2006]).				
Mixed Nociceptive/ Neuropathic Pain	A combination of the two types of pain. For example, patients with degenerative disc disease may suffer from mechanical (nociceptive) back pain and radicular (neuropathic) pain.				



CURRENT OPINION



Opioid-Induced Tolerance and Hyperalgesia

Sebastiano Mercadante 1,2 · Edoardo Arcuri 3 · Angela Santoni 4

Published online: 1 October 2019 © Springer Nature Switzerland AG 2019

Abstract

Opioids are very potent and efficacious drugs, traditionally used for both acute and chronic pain conditions. However, the use of opioids is frequently associated with the occurrence of adverse effects or clinical problems. Other than adverse effects and dependence, the development of tolerance is a significant problem, as it requires increased opioid drug doses to achieve the same effect. Mechanisms of opioid tolerance include drug-induced adaptations or allostatic changes at the cellular, circuitry, and system levels. Dose escalation in long-term opioid therapy might cause opioid-induced hyperalgesia (OIH), which is a state of hypersensitivity to painful stimuli associated with opioid therapy, resulting in exacerbation of pain sensation rather than relief of pain. Various strategies may provide extra-opioid analgesia. There are drugs that may produce independent analgesic effects. A tailored treatment provided by skilled personnel, in accordance with the individual condition, is mandatory. Any treatment aimed at reducing opioid consumption may be indicated in these circumstances. Interventional techniques able to decrease the pain input may allow a decrease in the opioid dose, thus reverting the mechanisms producing tolerance of OIH. Intrathecal therapy with local anesthetics and a sympathetic block are the most common techniques utilized in these circumstances.

Key Points

The development of tolerance is the main problem during opioid treatment as it requires increased opioid drug doses to achieve the previous level of analgesia.

Mechanisms of opioid tolerance include drug-induced adaptations or allostatic changes at the cellular, circuitry, and system levels.

Dose escalation in long-term opioid therapy might result in a state of hypersensitivity to painful stimuli, known as opioid-induced hyperalgesia (OIH), resulting in exacerbation of pain rather than pain relief.

Possible strategies to mitigate, reverse, or prevent opioidinduced tolerance and OIH are the use of adjuvant analgesics or opioid switching.

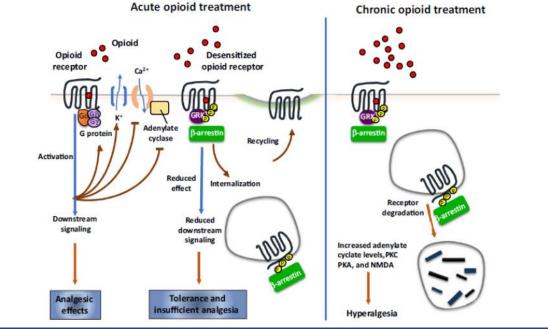
Pain and SUD (MOUD)

- Polysubstance use
- Altered nociocpetion threshold
- Physical dependence/tolerance
- Opioid-induced
 Hyperalgesia

1 Introduction

946 S. Mercadante et al.

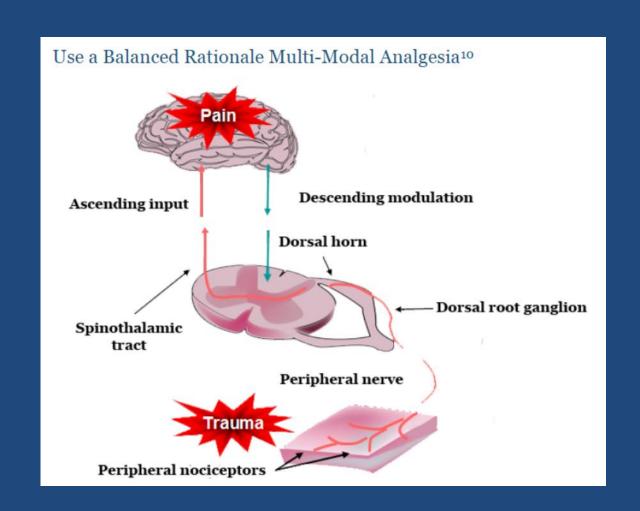
Acute opioid treatment Chronic opioid treatment



Acute Pain Should Be Treated

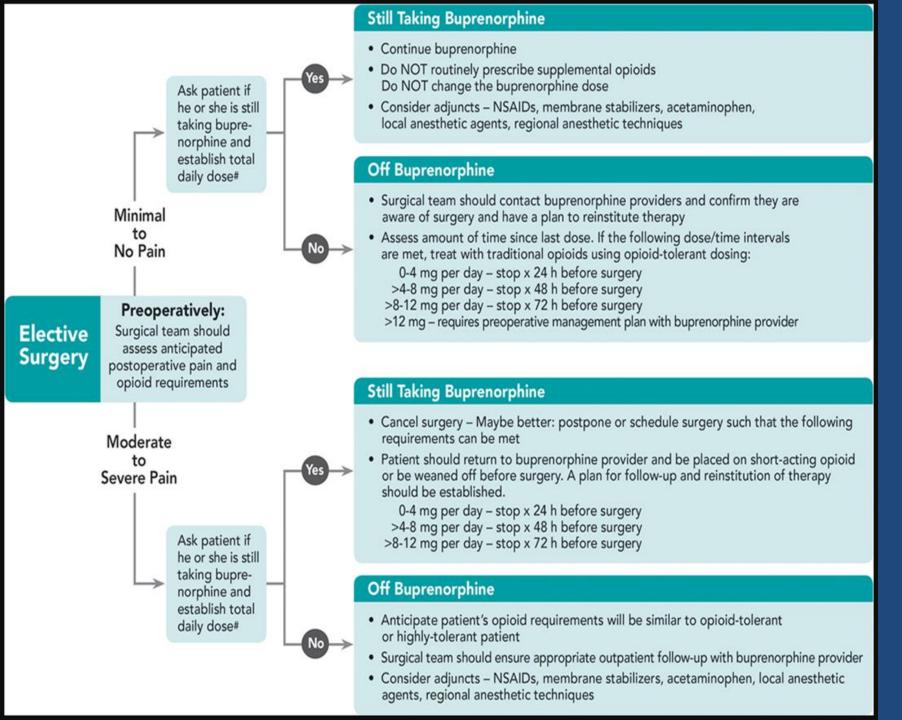
- MOUD is NOT analgesia
- People w MOUD have tolerance, likely need more analgesia
- Multi-modal therapy preferred
- If opioids used: oral over IV
- If opioid PCA: avoid basal infusion

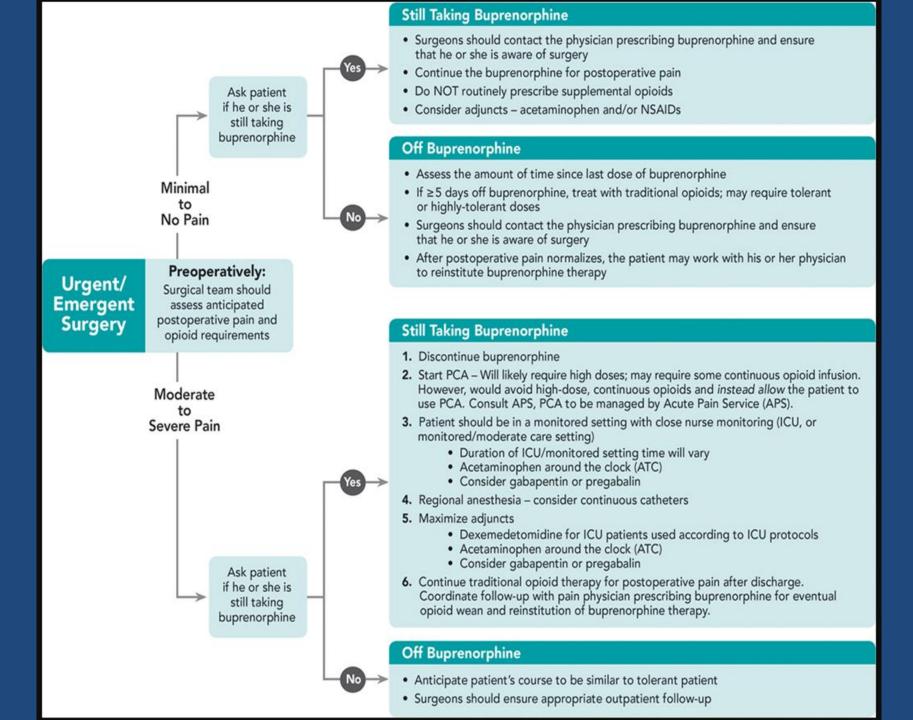
Consensus Statement: American Pain Society, ASRA and the American Society of Anesthesiologists



MOUD versus Analgesia Daily versus Split Dosing

- Analgesic effect: 6-8 hours (Bup and Methadone)
- Therefore Split Dosing
- However: Split dosing not possible from OTP







Acute Pain Management in Patients with Opioid Use Disorder

David Tauben, MD Jared W. Klein, MD Joseph O. Merrill, MD

Debra B. Gordon, RN, DNP, FAAN

Strategy	Suggested Phrasing
Validate patient's pain and frustration/fear/other emotions.	"I know that you're in pain and you're worried. We will do our best for your pain."
Review the data objectively.	"I see that you are able to function better and sleep better than before."
Set clear limits when responding to requests for inappropriate intravenous opioids which are not indicated.	"Our standard for all patients is to not give IV medication for people who are able to take pills" "It is not so important how we get the opioid into your body. What is more important is the right amount at the right time. Though IV may seem stronger it is really only faster but it will also wear off sooner than oral medicine. Oral medicine will give you more steady pain control."

<u>Use empathy.</u> When patient replies that nothing works except for the IV opioids.	"I'm really sorry you feel that way. This sounds like it is really terrible for you. I understand how it must be difficult to understand why we are saying no to more opioids, but we care about your safety. I know there are ways we can work together so you feel better"
Avoid arguing.	"There is no reason for us to argue about this" or "I am not going to argue with you."
Do not abandon the patient; commit to treating pain with non-opioid measures.	"I believe that you have pain, and I want to continue to work with you to treat the pain with other approaches"
Use risk/benefit language	"The risks of these medications are higher than the benefits for you"
Be empathetic when it is time to deny or stop opioids	"This must be very difficult for youIn my professional opinion (or medical research does not support), this type of pain medication, it is simply not safe for you in the long run" or "It may seem in the short run that opioids help, but they are not the best approach and can make your pain and problems worse over time"
Respond directly to threats to leave against medical advice	"You have the right to leave the hospital, but I still cannot give you inappropriate medications"

Table 1: Difficult Conversation Strategies and Suggested Phrasing



Pain Medicine 2011; 12: 996–1004 Wiley Periodicals, Inc.

REVIEW AND PRESIDENT'S

Long-Term Consequences o Mounting Evidence for Pain Disease and Parallels with C Disease States

Key W logical

Introdu

Chronic the Inter

that "pe

which is

of com

are ass

its treat

fibromya diabetic pain co

afflicting

When le

or dise

function pain ce

become

have bo

patients

increase

15]. Wh

more in

Consec

Patients

further o

physical

Impact

those w

associal

order [1

Perry G. Fine, MD

Department of Anesthesiology, School of Medicine, Pain Research Center, Salt Lake City, Utah, USA

Reprint requests to: Perry G. Fine, MD, Department of Anesthesiology, School of Medicine, Pain Research Center, Suite 200, 615 Arapeen Drive, Salt Lake City, UT 84108, USA. Tel: 801-585-7690; Fax: 801-585-7694; E-mail: perry.fine@hsc.utah.edu.

Disclosure: Nothing to disclose in relation to the contents of this paper.

Abstract

Objective. This article reviews the potential physical and psychological consequences of chronic pain and the importance of implementing effective therapeutic strategies to mitigate the harms associated with inadequate treatment.

Results. A review of recent literature examining the neurobiology and pathophysiology of chronic pain reveals that this highly prevalent condition negatively impacts multiple aspects of patient health, including sleep, cognitive processes and brain function, mood/mental health, cardiovascular health, sexual function, and overall quality of life. Furthermore, chronic pain has the capacity to become increasingly complex in its pathophysiology, and thus potentially more difficult to treat over time. The various health complications related to chronic pain can also incur significant economic consequences for patients.

Conclusions. Like other chronic conditions, it is important that chronic pain is managed with the objective of minimizing or avoiding its associated long-term sequelae. In line with this approach, early and effective multimodal treatment strategies, including analgesic therapy that controls pain intensity, are essential to improving outcomes and returning patients to normal levels of function.

Table 1 Prevalence of sequelae associated with chronic pain

Source	Condition	Chronic Pain (%)	Control (%)*	P/OR	
Altered mood Gureje et al., 1998	Anxiety or depressive disor	der 33.7	10.1	P < 0.001	
Ohayon et al., 2003 Von Korff et al., 2005	Table 3 Effects	s of pain control or	n various a	spects of patient he	alth
Kinney et al., 1993	1	Chronic Pain Condit	ion	Analgesics	Measures
Ratcliffe et al., 2008	Sleep	Osteoarthritis, low be chronic non-cance diabetic periphera neuropathy [67]	er pain,	Long-acting opioid, short-acting opioid	 Increased duration of sleep Improved overall sleep quality, sleep continuity, sleep architecture, composite pain, and sleep index score Less trouble falling asleep, need for sleep medication, awakening night/morning, interference of pain
Cognition, brain function Dick and Rashiq, 2007 Sleep Marty et al., 2008 Morin et al., 1998	Exercise performance	Fibromyalgia [68] Chronic back pain [6	59]	Antidepressant Opioid	Improved sleep Improved lifting performance Increased time to fatigue
McCracken and Iverson, 2002 Marin et al., 2006	Depression	Musculoskeletal pair Chronic non-maligna		Interventional treatment Sustained-release	 Improvement in depression on Patient-Health Questionnaire 9 Improved Beck Depression Inventory scores and incidence of normal mood
Cardiovascular health Bruehl et al., 2005	1	pain [71]		opioid	scores Reduced incidence of mood disturbances and borderline to extreme depression
Sexual function Ryan et al., 2008	Cognition	Chronic non-maligna pain [71]	ant	Sustained-release opioid	 Improved scores in cognitive function tests
Ambler et al., 2001 Shaver et al., 2006	Quality of life	Fibromyalgia [68]		Antidepressant	 Improved score on health-related quality of life
Quality of life and function McCarberg et al., 2008		Chronic non-maligna pain [72]	ant	Opioid	Improved physical and mental health on the SF-36
Smith et al., 2001	Reporting "long-term limitin illness" (SF-36) [27]		10.3	P < 0.001	
Sheu et al., 2008	Score ≥ 5 on 7 pain	26 (chronic	2.7 (pain but	not —	

chronic severe pain)

severe pain)

interference items [28]

Unless otherwise indicated, control groups are composed of patients without chronic pain.
 OR = odds ratio: CI = confidence interval.

Journal of Pain Research

Dovepress

open access to scientific and medical research

Off.2000

Open Access Full Text Article

REVIEW

A review of chronic pain impact on patients, their social environment and the health care system

This article was published in the following Dove Press journal: Journal of Pain Research 28 June 2016 Number of times this article has been viewed

María Dueñas¹ Begoña Ojeda² Alejandro Salazar² Juan Antonio Mico³ Inmaculada Failde²

'Nursing Faculty "Salus Infirmorum". The Observatory of Pain, University of Cádiz, Cádiz, Spain; 'Preventive Medicine and Public Health Area, The Observatory of Pain, University of Cádiz, Cádiz, Spain; 'Department of Neuroscience, Pharmacology, and Psychiatry, CIBER of Mental Health, CIBERSAM, Institute of Health Carlos III, University of Cádiz, Cádiz, Spain Abstract: Chronic pain (CP) seriously affects the patient's daily activities and quality of life, but few studies on CP have considered its effects on the patient's social and family environment. In this work, through a review of the literature, we assessed several aspects of how CP influences the patient's daily activities and quality of life, as well as its repercussions in the workplace, and on the family and social environment. Finally, the consequences of pain on the health care system are discussed. On the basis of the results, we concluded that in addition to the serious consequences on the patient's life, CP has a severe detrimental effect on their social and family environment, as well as on health care services. Thus, we want to emphasize on the need to adopt a multidisciplinary approach to treatment so as to obtain more comprehensive improvements for patients in familial and social contexts. Accordingly, it would be beneficial to promote more social- and family-oriented research initiatives.

Keywords: pain, everyday problems, social relationships, family environment, health services

Introduction

Chronic pain (CP) is recognized as a major public health problem, producing a significant economic and social burden. ¹⁻⁴ Moreover, this condition not only affects the patient (both as a sensory and emotional problem) but it also affects his/her family and social circle. ^{5,6} The biopsychosocial model, considered essential in pain, provides a framework for understanding how different diseases are related through an assessment of sensorial, cognitive/affective, and interpersonal factors. Thus, considering this framework, it has been shown that CP is often associated with other processes that, in turn, affect pain strongly⁷ (Figure 1).

Studies performed in different settings have demonstrated that CP affects between 10% and 30% of the adult population in Europe. 1.8 Indeed, a recent study showed a 16.6% prevalence of this condition among the general population in Spain, with at least one person affected in every four Spanish homes. 4 The experience of pain interferes with different aspects of the patient's life, 9 negatively affecting their daily activities, physical and mental health, family and social relationships, and their interactions in the workplace (Figure 1). This problem also affects the health care system and what is known as economic well-being, 1.9-15 the strong burden associated with CP not only deriving from health care costs but also from the loss of productivity and from compensatory payments to patients as a result of the disability that pain produces. 16

Dueñas et al

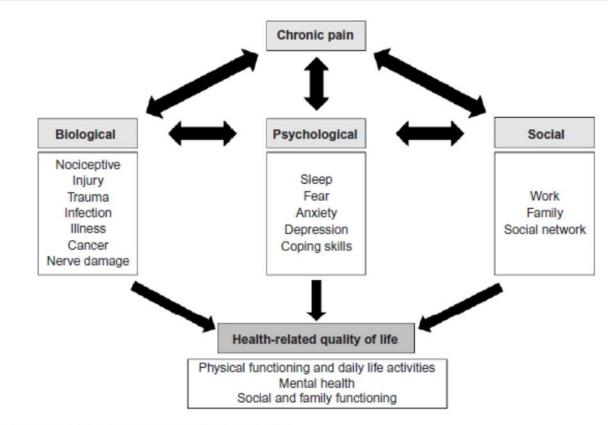


Figure 1 Biopsychosocial model of pain and consequences on the quality of life.

Correspondence: María Dueñas Nursing Faculty "Salus Infirmorum", The Observatory of Pain, University of Cádiz, C/Ancha, 29, 11001 Cádiz, Spain Email maria.duenasro@uca.es

A TREATMENT IMPROVEMENT PROTOCOL

Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders







Exhibit 3-1 Algorithm for Managing Chronic Pain in Patients With SUD

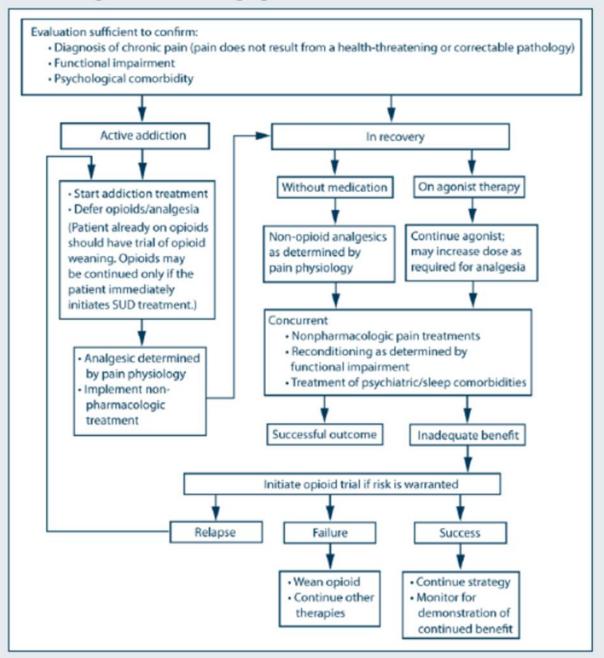


Exhibit 3-2 Summary of Non-Opioid Analgesics

Analgesic	Addictive	Notes
Acetaminophen	No	Should normally not exceed 4 g/day; in adults with hepatic disease, the maximum dose is 2 g/day. Potentiates analgesia without potentiating respiratory and sedative side effects.
NSAIDs	No	Are used to relieve numerous types of pain, espe- cially bone, dental, and inflammatory, and enhance opioid analgesia. May cause gastrointestinal bleed- ing and renal insufficiency.
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	No	Are used to relieve several nonstructural types of pain (e.g., migraine, fibromyalgia, low back pain) and probably others.
Tricyclic Antidepressants	No	Have demonstrated efficacy in migraine prophylaxis, fibromyalgia, many neuropathic pains, vulvodynia, and functional bowel disorders. Watch for anticholinergic side effects and orthostatic hypotension (fall risk in older people).
Anticonvulsants	No	Some have demonstrated efficacy in relieving fibro- myalgia, migraine prophylaxis, and neuropathic pains.
Topical Analgesics	No	Comprise several unrelated substances (e.g., NSAIDs, capsaicin, local anesthetics). Work locally, not systemically, and therefore usually have minimal systemic side effects.
Antipsychotics	No	Have no demonstrated analgesic effect, except to abort migraine/cluster headache. Risks include extrapyramidal reactions and metabolic syndrome.
Muscle Relaxants	Carisoprodol (Soma) is addictive. Some others have sig- nificant abuse potential.	Have not been shown to be effective beyond the acute period. Some potentiate opioids and are not recommended.
Benzodiazepines	Yes	Not recommended (see discussion).
Cannabinoids	Yes	Not recommended (see discussion).

Key Points

- · Pain treatment goals should include improved functioning and pain reduction.
- Treatment for pain and comorbidities should be integrated.
- Non-opioid pharmacological and nonpharmacological therapies, including CAM, should be considered routine before opioid treatment is initiated.
- Opioids may be necessary and should not be ruled out based on an individual's having an SUD history.
- The decision to treat pain with opioids should be based on a careful consideration of benefits and risks.
- Addiction specialists should be part of the treatment team and should be consulted in the development of the pain treatment plan, when possible.
- A substantial percentage of patients with and without SUDs will fail to benefit from prolonged opioid therapy, in which case it should be discontinued, as with any other failed treatment.

CDC Guideline for Prescribing Opioids for Chronic Pain



Morbidity and Mortality Weekly Report

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016



Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.htm



12 recommendations, including:

- Opioids not 1st line or routine therapy for chronic pain
- Use caution when increasing dosages, especially <a>>50
 mg*; avoid or justify escalating to <a>>90 mg
- No more than needed for acute pain; 3-7 days usually enough
- Check Prescription Drug Monitoring Program (PDMP) for other prescriptions, high total dosages
- Avoid concurrent benzodiazepines and opioids
- Offer or arrange medication-assisted treatment for opioid use disorder

^{*}in morphine equivalents

APPS & RESOURCES FOR RELAXATION

Happify: for Stress & Worry



Happify provides activities and games that can help you overcome negative thoughts, stress, and life's challenges for improved emotional health. \$15/month

Headspace: Meditation & Sleep



Headspace provides guided meditation with the goal of mindfulness to help people stress less, focus more and sleep better. Headspace is offering FREE resources during the current global crisis.

Self-help for Anxiety Management: SAM



SAM offers a range of self-help methods for people who are serious about learning to manage their anxiety. Free.

Anxiety Free: iCan Hypnosis



iCan can be used to learn self-hypnosis techniques to help people relax and have more subconsciously peaceful thoughts.

Insight Timer



Insight Timer provides guided meditations, music tracks and ambient sounds to calm the mind, focus, sleep better, and relax.

Free.

White Noise



White Noise: The FREE version offers a variety of soothing noises to help meditate or decompress. Set the timer, close your eyes and breathe for a quick opportunity to re-center and return to present.

Waking Up: A Meditation Course



Waking Up provides different styles of guided meditation lessons for the purpose of living a more balanced and fulfilling life. \$8.33/month

Calm: Meditate, Sleep, Relax



Calm provides guided meditations, sleep stories, breathing programs, stretching exercises, and relaxing music to help people experience better sleep, lower stress, and lessen anxiety. \$14.99/month

Interventions for Chronic Pain

Cognitive therapy

Monitor thoughts and feelings

Attention diversion/distraction

Imagery and Hypnosis

Behavioral therapy
Activity monitoring
Stress monitoring and reduction
Relaxation and Biofeedback

Substance Abuse, 33:361–365, 2012 Copyright © Taylor & Francis Group, LLC ISSN: 0889-7077 print / 1547-0164 online DOI: 10.1080/08897077.2011.638734



BRIEF REPORTS

Pain Is Not Associated with Worse Office-Based Buprenorphine Treatment Outcomes

Aaron D. Fox, MD Nancy L. Sohler, PhD, MPH Joanna L. Starrels, MD, MS Yuming Ning, PhD Angela Giovanniello, PharmD Chinazo O. Cunningham, MD, MS

ABSTRACT. Physical pain is common among individuals seeking treatment for opioid dependence. Pain may negatively impact addiction treatment. The authors prospectively studied opioid-dependent individuals initiating office-based buprenorphine treatment, comparing buprenorphine treatment outcomes (treatment retention and opioid use) among participants with and without pain (baseline pain or persistent pain). Among 82 participants, 60% reported baseline pain and 38% reported persistent pain. Overall, treatment retention was 56% and opioid use decreased from 89% to 26% over 6 months. In multivariable analyses, the authors found no association between pain and buprenorphine treatment outcomes. Opioid-dependent individuals with and without pain can achieve similar success with buprenorphine treatment.

KEYWORDS. Buprenorphine, chronic pain, opioid dependence

Drug and Alcohol Dependence 193 (2018) 131-136



Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep



Full length article

Substance misuse in patients who have comorbid chronic pain in a clinical population receiving methadone maintenance therapy for the treatment of opioid dependence



Cassie Higgins^{a,*}, Blair H. Smith^b, Keith Matthews^a

ARTICLEINFO

Scotland, UK

Eryword:
Opioid agonist therapy
Methadone maintenance therapy
Opioid dependence
Chronic pain
Illicit substance use

ABSTRACT

Aims: To compare specific substance misuse in treatment-seeking, opioid-dependent patients with and without comorbid chronic pain, and to assess the respective value of urinalysis and patient reports in assessing substance misuse.

Methods: Participants comprised a clinical population in a regional NHS Substance Misuse Service in the East of Scotland (N = 521). The Brief Pain Inventory – Short Form was used to assess pain, and the Maudsley Addiction Profile and urinalysis were used to assess substance misuse at study inception. Urinalysis was used to assess substance misuse during the 5-year follow-up period. Data were hosted, linked, anonymized and analyzed within a national Safe Haven.

Results: Compared with opioid-dependent patients with no pain, a significantly higher proportion of treatment-seeking, opioid-dependent patients with chronic pain were engaged in non-medical benzodiazepine use (69% versus 58%; p = 0.025) at study inception. Furthermore, a significantly higher proportion of this group was shown to continue non-medical benzodiazepine use (70% versus 42%; p = 0.037) and fillicit cannabinoid use (100% versus 31%; p = 0.002) the 5-year follow-up period. There were significant correlations between drug screen results and patient-reported use of opioids (Tetrachoric $\varrho = 0.4944$; p < 0.001), benzodiazepines (Tetrachoric $\varrho = 0.2834$; p < 0.001) and cannabinoids (Tetrachoric $\varrho = 0.8384$; p < 0.001).

Conclusions: Whilst gaining control of illicit opioid use during treatment, opioid-dependent patients with comorbid chronic pain demonstrated persistent problematic use of benzodiazepines and cannabinoids. This pattern of misuse was shown to persist during the 5-year follow-up period.

1. Introduction

Chronic pain is highly prevalent in treatment-seeking, opioid-dependent populations with between 36% and 68% affected (Barry et al., 2013; Tsui et al., 2016). Thus, chronic pain is an important clinical condition to be considered by addiction specialists. Furthermore, patients in receipt of opioid agonist therapy (OAT) who have comorbid chronic pain are associated with relatively poor health and substance use treatment outcomes, further complicating the delivery of effective treatment in substance misuse services. This comorbid presentation is associated with a range of medical and psychiatric morbidities (iskandar et al., 2013; O'Toole et al., 2013), in addition to relatively severe and enduring substance misuse problems (Dunn et al., 2014;

Larson et al., 2007). In addressing this issue, many studies have focused on any substance misuse (rather than specific drug misuse) as the target variable (e.g., Caldeiro et al., 2008) or illicit opioid use versus any other substance misuse (Dennis et al., 2015); however, there is a need to understand specific drug misuse profiles in this comorbid population to identify any patterns or problems with specific substances. Only then can further research explore the potential causes of the high levels of drug misuse in this comorbid group and work towards effective treatment delivery in substance misuse services.

OAT programs focus on a range of health-related and functional outcomes, but the core outcomes are considered to be retention in treatment and control over substance use (Kidd et al., 2013). These two core aims are considered to lead to decreased mortality (Cousins et al.,

https://doi.org/10.1016/j.drugalcdep.2018.08.038

Received 18 June 2018; Received in revised form 21 August 2018; Accepted 23 August 2018 Available online 18 October 2018

0376-8716/ © 2018 Elsevier B.V. All rights reserved.

Aaron D. Fox, Nancy L. Sohler, Joanna L. Starrels, Angela Giovanniello, and Chinazo O. Cunningham are affiliated with the Albert Einstein College of Medicine, Bronx, New York, USA; and the Montefiore Medical Center, Bronx, New York, USA.

Nancy L. Sohler is also affiliated with the Sophie Davis School of Biomedical Education, City College of the City University of New York, New York, New York, USA.

Yuming Ning is affiliated with the Montefiore Medical Center, Bronx, New York, USA.

Address correspondence to: Aaron D. Fox, MD, Clinical Instructor of Medicine, Albert Einstein College of Medicine, Montefiore Medical Center, 111 E. 210th Street, Bronx, NY 10467, USA (E-mail: adfox@montefiore.org).

This study was supported by HRSA (6H97HA00247); the CFAR at Einstein and Montefiore (NIH AI-51519); NIH R25DA023021; the Robert Wood Johnson Foundation; and CTSA grants UL.1 RR025750, KL2 RR025749 and TL.1 RR025748 from the NCRR, a component of the NIH. A portion of this work was presented at the Society of General Internal Medicine Annual Conference on May 5, 2011 in Phoenix, Arizona. The authors thank Mia Brisbane and Johanna Rivera for their help conducting this research.

Division of Neuroscience, University of Dundee, Mailbox 6, Level 6, Laboratories Biock, Ninovells Hospital and Medical School, Dundee, DD1 98Y Scotland, UK
Division of Population Health Sciences, University of Dundee, Mackenzie Bulding, Kirsty Semple Way, Ninewells Hospital and Medical School, Dundee, DD2 4RB

^{*}Corresponding author at: Division of Neuroscience, University of Dundee, Mailbox 6, Level 6, Laboratories Block, Scotland, UK.
E-mail addresses: c.y.higgins@dundee.ac.uk (C. Higgins), b.h.mith@dundee.ac.uk (B.H. Smith), k.matthews@dundee.ac.uk (K. Matthews).



Original Investigation

Cannabinoids for Medical Use A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

JAMA. 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358 Last corrected on November 5, 2015.

Figure 2. Improvement in Pain

Improvement in Pain With	Canna	binoid Events	Placel	oo Events	Odds Ratio	Favors :	Favors	
Cannabinoid vs Placebo by Study	No.	Total No.	No.	Total No.	(95% CI)	Placebo	Cannabinoid	Weight, %
Tetrahydrocannabinol (smoked)						•	1	
Abrams et al,77 2007	13	25	6	25	3.43 (1.03-11.48)	-	-	6.51
Nabiximols								
GW Pharmaceuticals, ²² 2005	54	149	59	148	0.86 (0.54-1.37)		-	19.02
Johnson et al, ⁶⁹ 2010	23	53	12	56	2.81 (1.22-6.50)			10.87
Langford et al,65 2013	84	167	77	172	1.25 (0.81-1.91)	· +	-	20.19
Nurmikko et al, ⁷⁶ 2007	16	63	9	62	2.00 (0.81-4.96)	·	-	9.84
Portenoy et al, 67 2012	22	90	24	91	0.90 (0.46-1.76)		+	14.04
Selvarajah et al, 70 2010	8	15	9	14	0.63 (0.14-2.82)	•	 	4.63
Serpell et al,88 2014	34	123	19	117	1.97 (1.05-3.70)		-	14.91
Subtotal 12 = 44.5%, (P = .0.94)	241	660	209	660	1.32 (0.94-1.86)			93.49
Overall 12 = 47.6%, (P = .0.64)	254	685	215	685	1.41 (0.99-2.00)			100.00
						0.2	10	
						Odds Ra	atlo (95% CI)	

INVITED REVIEW

Cannabinoids for the Treatment of Chronic Non-Cancer Pain: An Updated Systematic Review of Randomized Controlled Trials

M. E. Lynch 1,3 · Mark A. Ware2

Received: 29 January 2015 / Accepted: 5 March 2015 © Springer Science+Business Media New York 2015

Abstract An updated systematic review of randomized controlled trials examining cannabinoids in the treatment of chronic non-cancer pain was conducted according to PRIS MA guidelines for systematic reviews reporting on health care outcomes. Eleven trials published since our last review met inclusion criteria. The quality of the trials was excellent. Seven of the trials demonstrated a significant analgesic effect. Several trials also demonstrated improvement in secondary outcomes (e.g., sleep, muscle stiffness and spasticity). Adverse effects most frequently reported such as fatigue and dizziness were mild to moderate in severity and generally well tolerated. This review adds further support that currently available cannabinoids are safe, modestly effective analgesics that provide a reasonable therapeutic option in the management of chronic non-cancer pain.

Introduction

Chronic pain is a growing public health problem affectin approximately one in five people and predicted to it crease to one in three over the next two decades (Blyt et al. 2001; Moulin et al. 2002; Breivik et al. 2006). The prevalence of chronic pain is likely to increase as the population ages and as medical advances continue to in prove survival related to cancer, serious injury and diseases that previously would have been fatal, such a HIV, but have left the survivors with serious neuropathic pain conditions (Lynch 2011). Currently available agen (eg. antidepressant and anticonvulsant analgesics, opioid and nonsteroidal anti-inflammatory drugs) (Finnerup et a 2010) are inadequate to control all pain or are associate

Fig. 2 PRISMA flow diagram Additional records identified through other sources Records identified through (Google scholar n = 57) database searching (n = 201)Records after duplicates removed (n = 199)Records screened Records excluded (n = 199)(n = 186)Full-text articles assessed Full-text articles excluded, foreligibility with masons (n = 13)(n =1 pain was not an outcome; 1 was included in previous review) Studies included in validity assessment (n = 11)Studies Included in qualitative synthesis and data extraction (n = 11)

Conclusions

- Pain is common among people with addiction and can be managed
- OUD treatment outcomes not worse for those w chronic pain
- Split dosing and multi-modal interventions are key
- Cannabinoids hold promise for treatment of pain
- Person-centered care essential for both addiction and pain managment

Questions